IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

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| VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA LTD., and VIFOR FRESENIUS MEDICAL CARE RENAL PHARMA FRANCE S.A.S., | ) | |
| Plaintiffs, | ) | |
| v. | ) | C.A. No. 18-390-MN |
| TEVA PHARMACEUTICALS USA, INC., | ) | |
| Defendants. | ) | |

**DEFENDANT'S CORRECTED OPENING POST-TRIAL BRIEF ON INVALIDITY**


John W. Shaw (No. 3362)
Karen E. Keller (No. 4489)
Nathan R. Hoeschen (No. 6232)
SHAW KELLER LLP
I.M. Pei Building
1105 North Market Street, 12th Floor
Wilmington, DE 19801
(302) 298-0700
jshaw@shawkeller.com
kkeller@shawkeller.com
nhoeschen@shawkeller.com
*Attorneys for Defendant Teva Pharmaceuticals USA, Inc.*

OF COUNSEL:
Scott J. Bornstein
Richard C. Pettus
Jonathan D. Ball
GREENBERG TRAURIG LLP
MetLife Building
200 Park Avenue
New York, NY 10166
(212) 801-2172

Jonathan R. Wise
GREENBERG TRAURIG LLP
2700 Two Commerce Square
2001 Market Street
Philadelphia, PA 19103
(215) 988-7850


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## I. INTRODUCTION

Defendant Teva Pharmaceuticals USA, Inc. ("Teva") submits this Opening Post-Trial Brief on the issues of patent invalidity pursuant to D.I. 293. Based on the evidence presented at trial, asserted claims 29, 30, 33 and 56 ("the Asserted Claims") of U.S. Patent No. 9,561,251 (the "'251 patent") should be found invalid as obvious under 35 U.S.C. § 103. Claims 29 and 30 should also be found invalid under 35 U.S.C. § 112 for lack of enablement.

At trial, Teva established that the Asserted Claims were obvious in view of Orange Book-listed U.S. Patent No. 6,174,442 (the "'442 patent") alone or in combination with other prior art references such as the published Hergesell clinical study. The Asserted Claims of the '251 patent merely recite the sucroferric oxyhydroxide composition of Example 1 of the '442 patent, its inherent chemical properties, and a well-known dosage form (chewable tablet), all of which were disclosed and/or suggested by the prior art. Plaintiffs did not meaningfully dispute the substance of the prior art teachings and suggestions. Instead, Plaintiffs pinned their rebuttal on a legally and factually flawed argument that a person of ordinary skill in the art ("POSA") would not have "selected" Example 1 of the '442 patent. But, a "lead compound" approach is inapplicable to this case, and Example 1 is one of only a "finite number" that would have at least been obvious to try.

Similarly, Plaintiffs did not meaningfully challenge the evidence that the inherent properties of the Example 1 composition render obvious claims 29 and 30. Instead, Plaintiffs relied on attorney argument—without *any* evidentiary basis—that an unclaimed manufacturing variable (spray drying) ***may*** have impacted the inherent properties of the prior composition ("PA21") that was tested in the '442 patent and Hergesell. Despite having access to millions of pages of product development documents, as well as company witnesses and multiple technical experts, Plaintiffs did not present any evidence that spray drying had any impact on the iron release or absorption

properties of the prior art sucroferric oxyhydroxide composition. The Federal Circuit has soundly rejected such an unsupported, speculative approach to rebutting inherency.

Finally, claims 29 and 30 are also invalid under 35 U.S.C. § 112 for lack of enablement. The full scope of the broadly claimed functional limitations are not enabled in view of the large number of candidates within that claim scope, and the absence of guidance in the patent, which necessitates an undue level of experimentation for a POSA to make and screen each candidate to determine which ones exhibit the claimed functional properties. Plaintiffs' arguments as to alleged unpredictability of these claims based on the brand of starch stabilizer, individual patient attributes, and other factors confirm non-enablement because none of that information is in the '251 patent.

## II. THE ASSERTED CLAIMS ARE OBVIOUS

### A. The Asserted Claims Are Obvious in View of the '442 Patent

"Section 103(a) forbids issuance of a patent 'when the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.'" *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007). Prior art may be combined with the knowledge and experience of a POSA to "fill in the gap when limitations of the claimed invention are not specifically found in the prior art." *Belden Techs., Inc. v. Superior Essex Commc'ns LP*, 802 F. Supp. 2d 555, 563 (D. Del. 2011); *see also Randall Mfg. v. Rea*, 733 F.3d 1355, 1362 (Fed. Cir. 2013) ("[T]he knowledge of such an artisan is part of the store of public knowledge that must be consulted."). The evidence at trial established that the Asserted Claims would have been obvious to a POSA based on the teachings and suggestions of the '442 patent in light of the general knowledge of a POSA. (Tr. 289:17-303:22, 329:21-333:9, 335:4-16, 340:14-348:3.) *See Game & Tech. Co. v. Activision Blizzard Inc.*, 926 F.3d 1370, 1381

(Fed. Cir. 2019) ("[A] patent can be obvious in light of a single prior art reference if it would have been obvious to modify that reference to arrive at the patented invention."); *see also Koninklijke Philips N.V. v. Google LLC*, 948 F.3d 1330, 1338–39 (Fed. Cir. 2020) (affirming single reference obviousness "in light of a skilled artisan's general knowledge").

The testimony of Teva's expert, Dr. Chambliss, that a POSA (i.e., a pharmaceutical formulator) would begin with the '442 patent was undisputed. (Tr. 287:15-20, 288:21-289:2.) Instead, Plaintiffs argued that a POSA would not ***select*** Example 1 of the '442 patent—sucroferric oxy-hydroxide—as the "starting material" for formulation development, because Examples 6 and 8 allegedly provide marginally better phosphate adsorption. But, as explained below, such a "lead compound" analysis is not applicable in this case; and, in any event, it would have been obvious for a POSA to select Example 1 from the '442 patent's handful (i.e., a "finite number") of exemplary compositions.

**1. A "Dosage Form" of "at least 500 mg" and "about 800 mg" is Obvious**

At trial, Teva adduced evidence which showed that all of the limitations of the claims 1, 27, 32 and 55 (from which the Asserted Claims depend) were explicitly disclosed and/or suggested by the '442 patent. Plaintiffs did not contest this evidence with the exception of the limitation in claims 1 and 27 calling for a single "dosage form" containing "at least 500 mg[1]" of iron oxy-hydroxide. A POSA would understand the '442 patent's teaching of a "preferred" daily dose of 1.5 g of iron to equal an individual dose of 500 mg of iron (i.e., 800 mg of iron oxy-hydroxide) that would be administered 3-times per day with meals.[2] (Tr. 301:7-302:6, 335:4-16; JTX-3 at

[1] "700 to 1700 mg" in Claim 55 and "about 800 mg" in Claim 56.

[2] Dr. Chambliss' calculations of the preferred individual dose of 500 mg of iron (i.e., preferred daily dose of 1.5 g ÷ 3 x per day with meals = 500 mg/individual dose), and its conversion to 800 mg of iron oxyhydroxide, were not disputed at trial. (Tr. 291:7-292:1, 301:25-302:6, 698:16-699:2.)

3:19-21; PTX-217.1.) Indeed, this was clearly established by the '442 patent, as well as a POSA's general knowledge, that phosphate binders are administered 3-times daily with meals. (*Id*.; Tr. 730:11-16, 713:10-714:8; PTX-544.1 (instructing to "[d]ivide the total daily dose of FOSRENOL" of 1500 mg [i.e., the same amount as the '442 patent] and take "with or immediately after meals"); PTX-211.1 (take "with each meal" (PHOSLYRA 1990)); PTX-217.1 (take "three times per day with meals" (Renvela 2000)); PTX-214.1 ("three times per day with meals" (Renagel 2000)).) Plaintiffs' expert, Dr. Williams, conceded that the state of the art recognized that at least 500 mg was required to treat hyperphosphatemia. (Tr. 706:17-21.)

Plaintiffs' dispute with respect to obviousness of the "dosage form" limitation was based solely on attorney argument that a POSA would not put 500 mg of iron (800 mg of iron oxy-hydroxide) into a *single* dosage form. However, the evidence was clearly to the contrary. A POSA would have been motivated to include at least 500 mg or more in a single dosage form in the manner explicitly identified by the '442 patent in the sentence immediately preceding the dosage disclosure—"tablets … or contained in sachets, for example"—in order to reduce patients' pill burden, consistent with the general knowledge in the field at the time of the invention (i.e., 2007).[3] (*Id*.; JTX-3 at 3:9-21; Tr. 297:21-298:8, 303:23-304:2, 337:11-339:3, 456:24-461:16, 713:10-714:18; PTX-544.1 (FOSRENOL 500 mg, 750 mg and 1000 mg chewable tablets); DTX-120.1 (Renvela 800 mg tablet or powder); JTX-7.2; JTX-4 at 6:56-59, claim 1.)

The evidence was also clear that a POSA would have had a reasonable expectation of success of being able to formulate a single dosage form of at least 500 mg using the "powder" of

[3] Plaintiffs did not present any evidence or cogent reasoning in support of their argument that a POSA might instead prefer to use multiple dosage forms with a given meal. Plaintiffs also presented no evidence as to any alleged criticality or unexpected results associated with either of the claimed "at least 500 mg" or "about 800 mg" amounts.

Example 1, especially given the '442 patent's affirmative statement that they "can" be formulated "as such or together with customary drug additives, such as customary carriers or auxiliary materials," including "as granules, tablets, dragees or contained in sachets." (*Id.*; JTX-3 at 3:9-20; Tr. 704:13-25, 296:16-298:8, 332:3-20.) Plaintiffs did not challenge the feasibility of doing so. Thus, the evidence showed that the "at least 500 mg" (claims 29, 30 and 33) and "about 800 mg" (claim 56) limitations would have been obvious over the '442 patent.

**2. The "Chewable Tablet" Limitation of Asserted Claim 33 Is Obvious**

Claim 33 adds only that the composition of claim 1 is a "chewable tablet." (Tr. 365:3-6.) No formulation or tablet details are claimed or otherwise required. (Tr. 739:16-25, 701:3-20.) Rather, the chewable tablet of claim 33 is merely a common sense and obvious choice of dosage form. (Tr. 363:11-376:18.) Neither Plaintiffs nor their expert disputed that chewable tablets were known or used in the prior art, or that a POSA would be able to make one from the powder of Example 1 of the '442 patent. Nor could they, because the prior art upon which they relied at trial confirms that chewable tablets "have been part of the pharmacist's armamentarium for a very long time." (DTX-39.3) and the '442 patent teaches that the composition "can" be made into "tablets" with the possible addition of just "customary drug additives."[4] (JTX-3 at 3:10-18.)

A POSA would view chewable tablets as the logical choice, given that tablets with this much sucroferric oxyhydroxide would be large and difficult to swallow. (Tr. 325:4-326:3, 365:15-366:8.) It would also be known that, since tablet size is not a concern for chewable tablets, the full amount could be included in a single dosage form and thereby "reduce overall pill burden—an important issue affecting patient compliance." (*Id.*; JTX-4 at 13:21-22.) Further, chewable tablets

[4] Which is exactly what both Vifor and Teva were able to do, i.e., make chewable tablets containing sucroferric oxy-hydroxide using only "common" additives. (Tr. 67:16-69:5; DTX-171.46; DTX-65.5; DTX-67.66; DTX-75.33; PTX-322.12.)

were known to require less water intake—a desirable benefit for patients with hyperphosphatemia. (Tr. 365:15-366:8.) Indeed, Plantiffs' cited prior art confirmed these motives. (DTX-39.3 (chewables improve "patient convenience through the elimination of the need for water for swallowing"); DTX-1006.21 (especially for patients who "may have difficulty swallowing solid dosage forms.").) Thus, the '442 patent suggested a chewable tablet to a POSA based on its teaching of a "tablet" dosage form, and the general knowledge of the associated advantages.

At trial, Plaintiffs' rejoinder was that a POSA *could* have difficulties formulating a chewable tablet due to possible "bad taste" or powder "flowability" issues. (Tr. 693:6-20.) Dr. Williams admitted, however, that he had no prior experience with iron oxy-hydroxides, nor any evidence supporting either position. (Tr. 700:25-701:2, 715:14-18.) He also conceded that neither of those considerations are claimed in the '251 patent (Tr. 701:6-20) and, that he did not consider record evidence that sucroferric oxy-hydroxide did not require taste masking but was, in fact, "[s]lightly sweet." (Tr. 717:22-718:25 ("[I]t has saccharose in it, I can see how it could be slightly sweet"); PTX-323.13.) Not surprisingly, Dr. Williams also failed to mention that his own cited prior art described sucrose (used in the '442 patent's Example 1) as one of the most well-known chewable tablet excipients for addressing taste and palatability issues, including in combination with starch. (DTX-39.12-13; DTX-1006.26, 29-30; Tr. 716:4-6, 478:5-12.) Similarly, with respect to powder flowability, Dr. Williams' cited prior art describes starch as a commonly used excipient known to "create desired bulk, flow properties, and compression characteristics of tablets." (DTX-1006.26-27.) He also did not consider Plaintiffs' regulatory submissions, which state that it is the starch in sucroferric oxy-hydroxide which "results in a free-flowing powder and allows . . . manufacture of the final drug product (i.e., tableting)." (PTX-323.12; Tr. 717:13-21 (conceding starch was added "to improve flowability"); DTX-82.13; DTX-67.24; DTX-65.3 ("Since this

mixture [sucrose only] cannot be directly applied to an industrial process, starch is added to promote free flowing characteristics"); DTX-75.26, 37.)

Thus, a POSA would have had every expectation of being able to make a chewable tablet from Example 1—"as such" or with nothing more than the "widely used," "standard," "usual," and "common" excipients used by Plaintiffs and Teva (DTX-65.5-7; DTX-67.65-66; DTX-75.33; DTX-77.58; PTX-322.12; DTX-171.46)—exactly as the '442 patent unequivocally states "can" be done (JTX-3, 3:9-20) and consistent with Dr. Williams' cited prior art. (DTX-39.21 ("With perseverance, nearly any drug can be formulated in chewable form to produce an elegant pharmaceutical that can be conveniently used by the public young and old alike.").)

Accordingly, the evidence at trial showed that the '442 patent suggested, and that a POSA would have had the motivation and reasonable expectation of being able to make, the exemplary high load compositions of the '442 patent into a tablet form that was chewable.

### 3. The "Essentially Non-Bioabsorbable" and Iron "Release Rate" Limitations of Claims 29 and 30 are Obvious

Claim 29 and 30's "essentially non-bioabsorbable" and iron "release rate below 2.5%" limitations were also taught and suggested by the '442 patent, which states that the "stabilized beta-iron oxy-hydroxide" compositions were "insoluble" and "have the advantage that … they release little iron." (JTX-3 at 2:58-62.) This express disclosure, and the corresponding expert testimony as to the reasonable expectation it gave to a POSA, was not rebutted by Plaintiffs' experts at trial. (Tr. 289:17-290:4, 299:5-300:24, 345:8-19, 356:5-16, 393:10-396:5.)

With respect to Claim 29, Plaintiffs' expert, Dr. Rastogi, relied on a description of Teva's ANDA product as "insoluble" as showing infringement. (Tr. 102:11-19.) Plaintiffs cannot have it both ways. To the extent the word "insoluble" can be relied on for purposes of infringement as showing/meaning that Teva's ANDA Product is "essentially non-bioabsorbable," it should be

afforded the same meaning and effect in the '442 patent for purposes of obviousness.[5]

Rather than presenting an affirmative evidentiary challenge with respect to claim 30, Plaintiffs instead tried to impose an anticipation standard as to whether the explicit statement in the '442 patent that the compositions were "insoluble" and "released little iron" would have necessarily disclosed a "release rate of 2.5%" to a POSA. But, that is not the standard. *See Merck & Co. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807-08 (Fed. Cir. 1989) ("Unlike a section 102 defense … the question under 35 USC 103 is not merely what the references expressly teach but what they would have suggested to one of ordinary skill in the art at the time the invention was made.") Plaintiffs' position "improperly equates a reasonable expectation of success with absolute certainty." *See Hospira, Inc. v. Amneal Pharm., LLC*, 285 F. Supp. 3d 776, 794 (D. Del. 2018); *see also In re Copaxone Consol. Cases,* 906 F.3d 1013, 1026 (Fed. Cir. 2018) ("[o]bviousness does not require absolute predictability of success.").

The evidence at trial showed that the '442 patent suggested the claimed subject matter and that a POSA would have had a reasonable expectation of achieving it. (Tr. 345:8-19, 356:5-16.) This is particularly so in this case where there is no evidence in the record as to any alleged criticality of, or unexpected results associated with, the claimed value of "below 2.5%." *See Gentiluomo v. Brunswick Bowling & Billiards Corp*., 36 Fed. App'x 433, 438 (Fed. Cir. 2002) (finding the patentee "must show that the particular range is critical, generally by showing that the claimed range achieves unexpected results relative to the prior art range" and that "the invention would have been prima facie obvious because an ordinary skilled artisan would have sought the optimum values for the variable."). Indeed, with respect to alleged "unexpected results," Dr.

[5] The fact that iron oxy-hydroxides did not raise iron absorption concern due to their insolubility was within the general knowledge of a POSA. (JTX-3 at 2:1-8, 2:14-23, 4:15-19; Tr. 300:5-24.)

Rastogi admitted to addressing "not the exact number of 2.5 percent"; instead, he tracked ***verbatim*** the '442 patent's teaching that "very little, if any, iron is released." (Tr. 521:20-25, 525:24-526:9.) This testimony not only failed to overcome Teva's *prima facie* showing, but squarely aligned with and further supported the invalidating teachings of the '442 patent. (Tr. 356:24-357:5.) *See Gentiluomo*, 36 Fed. App'x at 436 ("in order to base a claim of patentability on the precise specific gravities … Plaintiff must demonstrate that the claimed range of specific gravity values … is critical and thus produces some unexpected result which differs from that outside the range.").

Accordingly, the unrebutted evidence presented by Teva at trial showed that Asserted Claims 29 and 30 would also have been obvious to a POSA in view of the teachings and suggestions of the '442 patent and the general knowledge in the field.

**4. Plaintiffs' Argument Concerning Selecting From a Handful of Examples in One Prior Art Reference Does Not Overcome Obviousness**

**a. A "lead compound" analysis is inapplicable as a matter of law**

Plaintiffs' "starting point" argument effectively asks the Court to apply a "lead compound analysis" under which Teva must show that a POSA would have selected Example 1 as a "starting point" (or lead compound) in order for the claims to be obvious. *See Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1291–92 (Fed. Cir. 2012) (indicating that in lead compound cases, a court first determines whether a POSA "would have selected the asserted prior art compounds as lead compounds, or starting points, for further development efforts."). But, such an approach is not applicable to Teva's obviousness argument based on the '442 patent.

In cases involving patentability of new chemical *compounds*—as opposed to the formulations at issue here[6]—"[w]hether a new chemical compound would have been prima facie

[6] Plaintiffs' expert, Dr. Williams, conceded at trial that the examples in the '442 patent all have the same active moiety, namely iron oxy-hydroxide, and that any remaining constituents in the

obvious over particular prior art compounds ordinarily follows a two-part inquiry." *Id.* at 1291. "First, the court determines whether a chemist of ordinary skill would have selected the asserted prior art compounds as *lead compounds*, or *starting points*, for further development efforts....The second inquiry in the analysis is whether the prior art would have supplied one of ordinary skill in the art with a reason or motivation to modify a lead compound to make the claimed *compound* with a reasonable expectation of success." *Id.* at 1291-92.

In this case, none of the Asserted Claims are *compound* claims—they are all composition or method claims, so a lead compound analysis is not applicable. *See Auxilium Pharm., Inc. v. Watson Labs., Inc.*, 2014 WL 9859224, at *13 (D.N.J. Dec. 16, 2014) ("This is not a chemical compound case—this case involves a pharmaceutical composition. Auxilium has failed to cite to any binding legal authority suggesting that the Court must use a reference composition framework in conducting an obviousness inquiry in a pharmaceutical composition case."); *Janssen Biotech, Inc. v. Celltrion Healthcare Co.*, 2018 WL 10910845, at *8–10 (D. Mass. July 30, 2018), *aff'd*, 796 F. App'x 741 (Fed. Cir. 2020) ("[T]he court finds that it is not required to apply the lead compound analysis, and its requirement of motivation to select a particular prior art compound that was a preferable starting point compared with other compounds in the art, in this case, which involves mixtures of known ingredients, such as the claimed compositions.")[7] Accordingly, Plaintiffs' "lead compound analysis" or starting point argument should be rejected. *Id.*

**b. The law does not require a POSA to select from amongst the '442 patent's "finite number" of examples**

examples are merely "excipients." (Tr. 705:18-706:13.) As such, the "lead compound" would be iron oxyhydroxide in every relevant example from the '442 patent.

[7] A lead compound analysis is not applicable to "methods of using" (such as claim 56). *Novartis Pharm. Corp. v. W.Ward Pharm. Int'l Ltd.*, 923 F.3d 1051, 1060 (Fed. Cir. 2019) ("[The patent] does not claim the everolimus compound itself, but rather methods of using the compound. This case therefore does not require lead compound analysis.")

Even under Plaintiffs' "starting point" theory, the argument still fails because Example 1 is one of only a very small handful of compositions disclosed in the '442 patent for treating hyperphosphatemia.[8] On this, the law is also clear that where a composition is one of only a finite, small number of identified predictable solutions, it would at the very least have been obvious to try. *See Hoffmann-La Roche Inc. v. Apotex Inc.*, 748 F.3d 1326, 1332 (Fed. Cir. 2014); *see also C.W. Zumbiel Co., Inc. v. Kappos*, 702 F.3d 1371, 1387 (Fed. Cir. 2012) (obvious where "no more than the exercise of common sense in selecting one out of a finite—indeed very small—number of options"); *Purdue Pharma Prods. L.P. v. Par Pharm., Inc.*, 642 F. Supp. 2d 329, 368 (D. Del. 2009) ("[O]bviousness exists when a finite, and in the context of the art, small or easily traversed, number of options . . . would convince an ordinarily skilled artisan of obviousness.").[9]

It is also of no moment that Example 1 is not explicitly described as a "preferred" embodiment in the '442 patent. (Tr. 397:2-13.) *See Purdue*, 377 F. App'x at 982 (prior art "renders the selection of tramadol obvious regardless [of] whether or not the patent lists tramadol as a preferred embodiment."). The fact "[t]hat the [prior art] discloses a multitude of effective combinations does not render any particular formulation less obvious. This is especially true because the claimed composition is used for the identical purpose taught by the prior art." *Merck*, 874 F.2d at 807. Accordingly, the question of whether it would have been obvious to start with (or select) Example 1 is not the relevant inquiry.

[8] The '442 patent discloses a total of 5 compositions: (i) Example 1 (starch/sucrose, which was also used in Examples 2-5, 12, 13, and 16); (ii) Example 6 (sucrose); (iii) Example 7 (amylopectin); (iv) Example 8 (dextrin); and (v) Example 9 (humic acid). Of those, Plaintiffs essentially only point to Examples 6 and 8 as allegedly better "starting points" (Tr. 399:11-20, 662:21-664:16.) This and Plaintiffs' other teaching away argument is addressed in greater detail in Section II.B.4.

[9] This law is not at all inconsistent with a lead compound analysis even were it deemed applicable. *See AstraZeneca AB v. Aurobindo Pharma Ltd.*, 232 F. Supp. 3d 636, 647 (D. Del. 2017) ("the court concludes that a POSA would have considered P32/98 and NVP–DPP728 in addition to several other lead compounds.").

### B. All of the Asserted Claims Are Obvious in View of the '442 Patent in Combination with Hergesell and the Other Prior Art Presented at Trial

In addition to being obvious over the '442 patent alone, the evidence at trial also demonstrated that the Asserted Claims would have been obvious over the '442 patent in combination with Hergesell and the general knowledge of a POSA (as reflected in the '079 patent, the '465 patent, and Lieberman references). Dr. Chambliss testified that a formulator considering phosphate binding compositions of the '442 patent would look to the Hergesell clinical study—which, in turn, directs the reader back to the '442 patent for "production information" concerning the drug administered to patients[10]—for further clinical information. (Tr. 305:23-306:5.) A POSA would have likewise been motivated to combine the other prior art references—the '079 patent (iron oxyhydroxides for binding phosphate), '465 patent (high-load phosphate binders), and Lieberman (widely used treatise on formulation of dosage forms including high-load drug products)—with an expectation that the powder of the Example 1 composition could be formulated into a single dosage form having at least 800 mg of iron oxy-hydroxide, including a chewable tablet, and would meet the "essentially non-bioabsorbable" and "release rate" limitations of claims 29 and 30. The strong evidence of motivation to combine was not challenged. (Tr. 295:23-298:12, 303:23-304:24, 317:11-321:25, 330:24-347:14, 356:17-359:11, 367:9-376:18.)

#### 1. The Single Dosage Form Limitation is Obvious in View of the Prior Art Combination

As discussed above (pp. 3-5), the limitation of Claim 56 of "about 800 mg" (and "at least 500 mg" in Claims 29, 30 and 33) of iron oxy-hydroxide in a single dosage form was disclosed and suggested by the '442 patent. The backdrop to those teachings of the '442 patent was the

[10] Plaintiffs do not contest that the '442 patent contains the same disclosure as DE 195 47 356 (cited by Hergesell) and EP 0 868 125 (cited in the '251 patent) (Undisputed Fact Nos. 30-31.)

earlier ’079 patent, which already disclosed and suggested a “unitary solid dosage form such as a compressed tablet” containing “500 mg or more” of iron oxy-hydroxide in “each oral dose.” (JTX-5 at 3:36-55; Tr. 303:23-304:11, 337:11-338:2.) Dr. Williams conceded that the “state of the art” taught as much. (Tr. 706:17-21.) Likewise, Hergesell confirmed the general practice of administering a phosphate binder 3 times per day “with meals,” as well as doing so with a high load of iron oxy-hydroxide in a ***single*** dosage form (i.e., a sachet powder packet) containing approximately 800 mg of iron oxy-hydroxide.[11] (Tr. 304:12-305:14, 335:17-337:10; JTX-7.2.)

**2. The “Chewable Tablet” Limitation of Asserted Claim 33 is Obvious in View of the Prior Art Combination**

In addition to the ’442 patent rendering Claim 33’s chewable tablet obvious as discussed above (p. 5-7), it also does so in view of the other prior art teachings, suggestions and motivations. For example, the ’465 patent taught that chewable tablets are preferred for treating hyperphosphatemia and specifically disclosed chewable tablets with high active loads of 500 mg, 750 mg, and 1000 mg to achieve the disclosed benefits of reduced water intake and pill burden, both of which were recognized in the field as important issues for individuals suffering from hyperphosphatemia. (Tr. 369:22-370:6; JTX-4 at 3:9-15, 6:56-59, 13:21-22.)[12] Dr. Chambliss’ testimony concerning a POSA’s motivation and reasonable expectation of success with respect to a chewable tablet for a high load phosphate binder was essentially unrebutted. (*Id.*; Tr. 325:4-326:3.) Dr. Chambliss also explained how both Lieberman and the ’465 patent would have

[11] Per the unrebutted testimony of Dr. Chambliss, Hergesell taught and suggested a dosage form containing 500 mg of iron (i.e., 800 mg of iron oxy-hydroxide) based on the reported solubility testing of 500 mg of iron, which a POSA would have understood as a test of the administered dosage. (Tr. 335:17-337:10.) A POSA would also understand the Hergesell powder to contain approximately 21.2% iron (i.e., about 848 mg of iron oxy-hydroxide in a 2.5 g sachet), as that iron percentage was contained in every example of the ’442 patent. (*Id.*; Tr. 330:4-8.)

[12] The ’079 patent’s disclosure of a high load single dosage form “such as a compressed tablet” would have further suggested a chewable tablet form to a POSA. (JTX-5.3, 3:36-55.)

provided a reasonable expectation of success of making a chewable tablet from Example 1, as it already included starch (promoting flowability) and sucrose (acceptable taste). (Tr. 369:1-376:18; JTX-8.7, 9, 42; Tr. 462:23-465:16, 470:18-472:16.) Dr. Williams did not contest any of the above, or that sucroferric oxy-hydroxide would have a "[s]lightly sweet" rather than bad taste. (Tr. 718:5-25.) And, as discussed above (p. 7), and addressed by Dr. Chambliss (Tr. 738:19-739:15), the Swarbrick and Ansel references do not teach away from chewable tablets but actually provide further motivation and reasonable expectation of success. (DTX-39.21 ("With perseverance, nearly any drug can be formulated in chewable form to produce an elegant pharmaceutical that can be conveniently used by the public young and old alike.").) Thus, the evidence showed that the "chewable tablet" limitation of claim 33 was a routine, obvious choice based on the '442 patent in view of Hergesell, the '465 patent, and/or Lieberman.

**3. Obviousness of Claims 29 and 30 in View of the Prior Art Combination**

In addition to showing that the "essentially non-bioabsorbable" and iron "release rate below 2.5%" limitations of claims 29 and 30 were obvious from the '442 patent itself (pp. 7-9, *supra*), the evidence also showed the obviousness of those claims in light of Hergesell and the '079 patent. The '079 patent disclosed that iron oxy-hydroxides "exhibit low solubility in physiological fluids, including gastric juices, thereby lessening the probability of side effects due to absorption of solubilized iron compounds," and that "due to their low solubility, provide little risk of side effects," and thus "contribute little to the levels of soluble iron concentration." (JTX-5 at 2:20-23, 3:10-11, 4:15-20.) The expectation of a POSA, therefore, would have been that the iron oxyhydroxide of Example 1 would exhibit low iron absorption and release/solubility. The testimony of Dr. Chambliss concerning the same went unrebutted by any witness at trial. (Tr. 345:8-350:16, 356:5-360:6.) Dr. Harris—Plaintiffs' only expert who previously opined on the

issue—was not called at trial, and Dr. Williams did not offer any rebuttal testimony. The testimony of Dr. Chambliss was that Hergesell's *in vivo* test results showed the administered iron oxy-hydroxide from the '442 patent was not absorbed by patients in a clinically significant amount, and also independently provided a POSA with a reasonable expectation that the "insoluble" compositions of Hergesell and the '442 patent were "essentially non-bioabsorbable." (Tr. 317:11-318:17, 346:5-348:24, JTX-7.4 (Table 3 data reported as showing "No significant change of serum iron and serum ferritin concentrations"); JTX-3 at 2:58-62.)[13]

Likewise, the unrebutted testimony of Dr. Chambliss on claim 30 was that Hergesell's reported *in vitro* iron solubility result of 2.1% after 5 hours—taken with the '442 patent's teaching that all the disclosed compositions are insoluble and release little iron—would have taught or suggested that an iron "release rate below 2.5%" was achieved by the administered composition, and would have provided an expectation that it would be achieved by the compositions of the '442 patent, including Example 1. (JTX-7.4; Tr. 319:19-321:2, 356:8-359:11, 432:12-437:15, 477:19-25.) A POSA would have understood that the iron solubility testing (run at the same temperature and pH of 3) in Hergesell was more rigorous than the test required by the Court's claim construction and, thus, based on the iron release of 2.1% after 5 hours in Hergesell, a POSA would have had an expectation of achieving Claim 30's release rate of below 2.5%. (Tr. 356:5-359:11 ("If only 2.1 percent of the iron goes into solution after five hours in a solubility test, then less than 2.5 percent of iron would be released in a dissolution test at two hours."); Tr. 319:19-321:2.)

Accordingly, the trial evidence showed that the "essentially non-bioabsorbable" and

[13] To the extent there is any question as to Dr. Chambliss's interpretation of Hergesell, Plaintiffs' FDA documents confirm that they interpreted the Hergesell teachings the same way, i.e., as showing that "[clinically] [s]ignificant absorption of iron is not expected." (Tr. 319:7-18; DTX-83.9; DTX-67.126, 179; DTX-77.91 ("Ferritin levels did not differ significantly during the study" and "the potential for iron overload is expected to be low").)

"release rate" limitations of claims 29 and 30 would have been obvious in view of the '442 patent in combination with Hergesell and/or the '079 patent (and the general knowledge of a POSA).

#### 4. There is No "Teaching Away" that Makes Example 1 Not Obvious or Overcomes the Strong Motivations to Combine the Prior Art

##### a. The Hergesell "formula" did not teach away from Example 1

Plaintiffs pinned their obviousness rebuttal on an argument that a POSA would be dissuaded from using Example 1 of the '442 patent based on the other examples in the patent and a "formula" in the Hergesell medical article. (Tr. 305:23-307:12, 325:4-326:3, 328:3-329:5, 348:4-350:16, 374:24-375:9.) First, the Hergesell "formula" would not dissuade a POSA away from using the powder composition of Example 1. Per the unrebutted testimony of Dr. Chambliss, a POSA would have recognized the "formula" provided in Hergesell to be non-standard and erroneous. (Tr. 402:22-403:17.) On this, Dr. Chambliss and Plaintiffs' chemistry expert Dr. Harris were in agreement—which is presumably one of the reasons why Dr. Harris was not called at trial (despite being Plaintiffs' ***only*** expert to opine on the invalidity of claims 29 and 30). (Tr. 402:25-403:1.)[14] For example, neither expert understood the meaning of the "L" or "1/M" in the Hergesell formula. (Tr. 403:12-17.) As Dr. Chambliss explained, a POSA would have known that the Hergesell authors were medical doctors and not chemists and thus would not have relied on or given weight to the Hergesell "formula," especially in view of its clear errors. (Tr. 402:22-403:5.)

Further, even if the Hergesell formula would have been afforded some weight by a POSA, the non-iron oxy-hydroxide part of the formula—$C_6H_{10}O_5$—is consistent with carbohydrates used in the '442 patent examples, including the starch used in Example 1 (which is then used throughout the patent in Examples 2, 3, 4, 5, 12, 13 and 16) (Tr. 409:22-410:4.) As such, the formula does not

[14] Instead, Plaintiffs' called only Dr. Williams, who did not challenge or address the undisputed errors in the "formula" and had relied on Dr. Harris for his own opinions. (Tr. 667:15-372:12.)

exclude Example 1 for purposes of obviousness but, at most, would only exclude Examples 6 (using just saccharose) and 9 (using humic acid). (Tr. 409:12-21.) *See Syntex (U.S.A.) LLC v. Apotex, Inc.*, 407 F.3d 1371, 1380 (Fed. Cir. 2005) ("[A] prior art reference that does not specifically refer to one element of a combination does not, per se, teach away.").

Moreover, taking this even a step further for sake of argument, Example 7 (using amylopectin) exhibited far worse *in vitro* phosphate binding capacity than the other carbohydrate-containing compositions of Example 1 and 8. Dr. Chambliss also testified that he was unaware of any instances of amylopectin being used in a pharmaceutical formulation. (Tr. 480:20-25.) Thus, at most, if a POSA were to consider the erroneous formula, they would be directed to only *two* Examples—Example 1 (using starch, along with saccharose) and Example 8 (using dextrin)—both of which demonstrated essentially identical *in vitro* "inorganic" phosphate binding capacity (i.e., identical results at a pH of 3 and 8, with only insignificant difference at pH 5.5) (Tr. 398:18-23, 411:2-412:7.) Two essentially identical choices is about as "finite" a number of options as exists under the law,[15] and thus would have been obvious for a POSA to try.

**b. A POSA would have used Example 1 of the '442 Patent**

The evidence at trial confirmed the multiple reasons why a POSA reviewing the '442 patent would have chosen the stabilized powder of Example 1. In addition to being the ***first*** example in the patent (actually, the first 5 examples)—which in and of itself makes it the most likely place to start (Tr. 396:13-18)—the starch/sucrose stabilized Example 1 powder is also undeniably the predominant composition that is used again and again throughout the '442 patent. (Tr. 292:11-

[15] *See* pp. 10-11, *supra*; *see also Bayer Pharma AG v. Watson Labs., Inc.*, 874 F.3d 1316, 1327 (Fed. Cir. 2017) ("[T]he fact that there may be reasons a skilled artisan would prefer one over the other does not amount to a teaching away from the lesser preferred but still workable option," and the fact that "better alternatives exist in the prior art does not mean that an inferior combination is inapt for obviousness purposes.").

295:3, 397:2-13, 478:1-480:25.) Indeed, Example 1's process for making the iron oxy-hydroxide is used for all of the other examples. Its starch/sucrose stabilized powder is also specifically used in the next four examples of the '442 patent, including Examples 2 and 3 (in which it is tested for "inorganic" phosphate binding) and Examples 4 and 5 (in which it is tested for "organic" phosphate binding). Notably, Examples 4 and 5 are the ***only*** examples in which the inventors selected one of the disclosed compositions (i.e., Example 1) to be tested for organic phosphate binding. Then, after the next four alternative compositions (i.e., Examples 6 (sucrose only), 7 (amylopectin), 8 (white dextrin), 9 (humic acid)), Example 1 is used again in Examples 12, 13 and 16, which are likewise of particular note to a POSA because they are the ***only*** examples in which one of the one of the ''442 compositions (Example 1), was selected by the inventors to be combined with a calcium salt (JTX-3 at 3:63-4:5, 9:29-53; Tr. 412:11-413:8 (Example 13 adds calcium acetate to Example 1 in accord with the patent's teachings)), and to be compressed into chewable rat pellets and administered with food, in accord with the purpose of the invention and phosphate binders in general. (JTX-3 at 9:65-10:35.) Thus, the stabilized starch/sucrose powder of Example 1 was not only selected for use in the vast majority of the patent examples (8 out of 12 of the stabilized binder examples), but when it came time to choose one of the examples—for organic phosphate binding, or to be tested in combination with a calcium salt, or to be compressed and tested with food—the inventors ***selected*** Example 1. This would not have been lost on a POSA, who would have followed the inventors and made the same selection of Example 1.

Moreover, the trial evidence provided several additional reasons why a POSA would have had an informed preference for Example 1. First, Example 1 is the only composition that is specifically referred to as a "powder" (i.e., a dosage form), and Dr. Chambliss testified that a POSA would view it as the only one of the examples which would not require further formulation

development. (Tr. 290:15-293:3.) As explained by Dr. Chambliss, and confirmed by the record evidence, because Example 1 contains both saccharose *and* starch, a POSA would recognize it as having the best profile in terms of taste/palatability and processability/flowability. (Tr. 284:11-285:2, 461:23-462:1, 478:5-24.) For instance, a POSA would recognize—and quickly discover, as Plaintiffs did—that using sucrose alone as the only stabilization agent (as in Example 6) results in a composition that becomes too sticky during processing (Tr. 479:11-15; DTX-65.3; DTX-80.11-12; DTX-82.13) and, that the addition of starch (as in Example 1) would resolve that issue and result in a free flowing powder that is "ready to go," either "as such" (as in Hergesell) or with additional customary additives (as in Velphoro and Teva's ANDA product). (*Id.*)[16]

### C. Claims 29 and 30 are Obvious as Claiming Nothing More than the Inherent Properties of the Composition(s) of the '442 Patent

The trial record shows that the "essentially non-bioabsorbable" and "release rate" limitations of claims 29 and 30 are inherent properties of the Example 1 composition of the '442 patent. (Tr. 354:19-357:15, 307:13-19, 308:7-24, 317:4-321:2, 326:4-327:10, 350:17-354:8, 354:14-18, 359:12-360:14, 361:14-363:10, 394:9-14, 395:20-25, 477:19-25, 346:1-4.) As such, these claims "do[] not impose any additional requirement[s]" in the obviousness context. *Alcon Research, Ltd. v. Apotex Inc.*, 687 F.3d 1362, 1369 (Fed. Cir. 2012); *see also Persion Pharm. LLC v. Alvogen Malta Operations Ltd.*, 945 F.3d 1184, 1190 (Fed. Cir. 2019) ("[I]n the context of obviousness, the 'mere recitation of a newly discovered function or property, inherently possessed by things in the prior art, does not distinguish a claim drawn to those things from the prior art.'"); *Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1354 (Fed. Cir. 2012) ("an obvious

[16] A POSA would also recognize that white dextrin (Example 8) is not as sweet as saccharose, and that both dextrin and sucrose (Example 6) would, without the addition of starch, be less effective at preventing the iron oxy-hydroxide from destabilizing over time. (Tr. 479:21-480:3.)

formulation cannot become nonobvious simply by administering it to a patient and claiming the resulting serum concentrations.").

Dr. Chambliss offered unrebutted testimony that the claimed properties are the natural result of the Example 1 composition. (Tr. 289:17-290:4, 354:14-18.) The '442 patent discloses that "the absorption materials comprising insoluble stabilised polynuclear beta-iron hydroxide" are "***insoluble***"[17] and "release little iron." (JTX-3; Tr. 299:5-301:6.) Per Dr. Chambliss, the inherent insolubility of the stabilized iron oxy-hydroxide of the '442 is directly correlated with decreased iron absorption and low iron release. (Tr. 299:20-24.) These inherent properties are confirmed by Hergesell, which measured and reported both iron release and iron absorption for a "stabilized polynuclear iron oxy-hydroxide" of the '442 patent. (Tr. 304:25-306:22, 317:11-318:11; JTX-7.4.)

As the evidence established, this "stabilized polynuclear iron oxy-hydroxide" was PA21, Plaintiffs' internal designation for the Example 1 composition. For example, Dr. Philipp, Plaintiffs' 30(b)(6) and a named inventor of the '251 and '442 patents, confirmed that it is Example 1 of the '442 patent that corresponds to the drug substance administered in Hergesell, and was designated by Plaintiffs as PA21 (and subsequently as PA21-1). (Tr. 242:18-243:3, 255:3-6, 259:18-24, 266:14-21, 317:4-10.) Prior to this litigation, the fact that PA21 was tested in Hergesell—and was disclosed and tested in the '442 patent—was ***uniformly*** confirmed throughout Plaintiffs' internal documents, including their submissions to the FDA seeking approval for Velphoro. (DTX-47.6 ("PA21 …. Details are described in the patent or in a published study from Hergesell"); DTX-78.46-47, 460 ("PA21 … has been shown in prior in vitro studies [32] to have

[17] As discussed above, Plaintiffs cannot credibly argue that the insolubility of the '442 compositions is insufficient to establish inherency, while simultaneously relying on the alleged insoluble nature of Teva's ANDA product for infringement (Tr. 102:11-19.) For this reason alone, the evidence establishes that the '442 patent inherently discloses the limitations of the claims.

high phosphate-binding" and in a "published study conducted by Hergesell … [34]").) It was similarly confirmed by Dr. Philipp in a non-prior art (pre-litigation) article he co-authored with another co-inventor, in which they unequivocally stated that the '442 patent's "[*i*]n *vitro* data have indicated that PA21 has a high phosphate-binding capacity," and that Hergesell's patients "were given PA21." (DTX-62.1-2 and 7-8; Tr. 253:5-12.) Indeed, after reviewing all of the evidence, Dr. Williams ***admitted*** that the Hergesell product was the Example 1 composition. (Tr. 710:13-23.)

With respect to claim 29, as reported in Table 3, Hergesell measured serum ferritin and iron levels before, during, and at completion of the 28-day study, and found "no significant change of serum iron and serum ferritin concentrations." (JTX-7.4; Tr. 317:17-318:11.) Dr. Chambliss testified that a POSA would reach the same conclusion based on the Table 3 data. (Tr. 318:1-5; JTX-7.4.) He further testified that a POSA would understand these results to mean that there was no clinically significant absorption of iron oxyhydroxide because "you're not going to have clinically significant increase in iron if it's not going up." (Tr. 318:12-17.) His testimony was unrebutted. Notably, Plaintiffs relied on Hergesell in its FDA filings to claim that "[s]ignificant absorption of iron is not expected." (DTX-83.9; Tr. 318:18-319:18.) Plaintiffs' internal documents further confirm that PA21 (Example 1 of '442 patent) is inherently essentially non-bioabsorable. (Tr. 351:2-354:8; DTX-47.6; DTX-83.9; DTX-77.19; DTX-80.12.)[18]

Hergesell also showed that PA21's iron release rate meets claim 30. Hergesell discloses that "[i]ron solubility *in vitro* after 5 h at a final concentration of 500 mg Fe/l at 37°C varies

[18] The unrebutted evidence also showed that the '251 patent itself confirms that the stabilized beta-iron oxy-hydroxide of the '442 patent is not absorbed by the human body, that the "compositions of the invention" are purportedly new formulations of the stabilized iron oxyhydroxide of the '442 patent, and that "due to their chemical nature, the iron oxy-hydroxides used and administered in accordance with the present invention essentially are not absorbed by the human body, i.e. they are essentially non-bioabsorbable." (JTX-1 at 2:64-67, 2:57-65, 4:45-63, 11:39-43; Tr. 326:4-21.) Thus, Plaintiffs admitted in the '251 patent that claim 29 is inherently disclosed in the '442 patent.

between 0% (at pH 8) and 2.1% (at pH 3).” (Tr. 320:10-321:2; JTX-7.3-4.) Dr. Chambliss explained that this test is not only comparable to that required by the Court’s construction for Claim 30, but actually more stringent because Hergesell measured the soluble iron after 5 hours rather than at 2 hours. (Tr. 358:14-20, “[the] solubility test is telling you what the release test results would be”). Dr. Chambliss also explained that “if the drug is not soluble in the media, it’s not going to be released and dissolved in the media” (Tr. 319:24-321:2), and concluded that “less than 2.1 percent of the drug at two hours would have been released” under the Court’s construction of Claim 30. (Tr. 320:16-20.) That testimony was also unrebutted.

Plaintiffs did not contest that Example 1 is compositionally identical to the material used in Hergesell. Instead, they advanced attorney argument that the unclaimed *drying* equipment could somehow alter its bioavailability or iron release rate. Specifically, Plaintiffs contend that the PA21 used in Hergesell was spray dried, whereas the PA21 powder of Example 1 of the ’442 patent was dried by rotary evaporation. But, even if this were so, Plaintiffs presented *zero* evidence that such a difference in drying techniques has any impact on bioavailability or iron release rate. Plaintiffs made the tactical decision not to call their only expert on this issue, Dr. Harris, at trial and relied solely on conjecture and attorney argument to rebut the overwhelming evidence of inherency. Even accepting that Hergesell’s PA21 was in fact spray dried, there is no testimony or evidence that it would impact Example 1’s release rate or bioavailability. (Tr. 481:16-482:2.) If anything, the record evidence—including Plaintiffs’ NDA—confirms the contrary. (Tr. 481:16-483:14; DTX-73.11 (“Because the iron component of the [Drug Substance] is practically insoluble, the particle size of the DS has ***no impact on bioavailabilty***. The particle size distribution is narrow with low variability between batches due to the controlled spray drying step in the manufacturing process of the DS.”).)

The Federal Circuit recently rejected arguments very similar to Plaintiffs' spray drying theory in *Hospira, Inc. v. Fresenius Kabi USA*, a case having strong parallels to this one. 946 F.3d 1322, 1330 (Fed. Cir. 2020). The claim at issue recited a "liquid pharmaceutical composition" of dexmedetomidine that "exhibits no more than about 2% decrease in the concentration of dexmedetomidine," and the prior art included a dexmedetomidine drug marketed by Hospira's predecessor that expressly met all limitations except for the "about 2%" limitation. *Id.* at 1324-27. The District Court relied on non-prior art stability data from the parties' FDA filings to conclude that this limitation was an inherent feature of the prior art product. *Id.* at 1327-28. The Federal Circuit affirmed, rejecting Hospira's arguments that (1) the District Court improperly relied on non-prior art embodiments from the parties' FDA filings to prove inherency, and (2) those embodiments were made using a different manufacturing process than the prior art product, which may affect the drug stability. *Id.* at 1327, 1329. As to the first argument, the Federal Circuit explained that extrinsic evidence, including the patentee's non-prior art documents, "can be used to demonstrate what is 'necessarily present' in a prior art embodiment even if the extrinsic evidence is not itself prior art" because it can "help[] to elucidate what the prior art consisted of." *Id.* at 1329-30. On the second point, the Federal Circuit held that "***unclaimed manufacturing variables . . . do not, as a matter of law, preclude a finding of inherency***." *Id.* at 1330 (emphasis added). It noted that the asserted claim "is not a method[ nor] product-by-process claim, and there are no limitations . . . regarding the [product's] manufacturing process." *Id.* at 1330. Thus, because there was no evidence that an unclaimed manufacturing step would make a difference in the API's stability, the Federal Circuit affirmed the District Court's obviousness conclusion. *Id.*

Here, Plaintiffs likewise have offered no evidence that spray drying would alter the iron release or absorption characteristics of the Example 1 composition. Absent evidence that the

unclaimed spray drying makes any difference, Plaintiffs' argument must be rejected. *See id.*; *Acorda Therapeutics, Inc. v. Roxane Labs., Inc.*, 903 F.3d 1310, 1335-36 (Fed. Cir. 2018) (noting patentee "cites no support" that inherent properties would differ between prior art and claim).[19]

Finally, Plaintiffs' attempt to preclude Teva from relying on any non-public documents or testimony to show that the Example 1 composition inherently meets the limitations of claims 29 and 30 is improper as a matter of law.[20] In view of the unequivocal admission at trial by Plaintiffs' expert, Teva respectfully submits that the Court need not reach the issue of whether it may rely on non-public or non-prior art documents. (Tr. 710:13-23.) Nevertheless, the law is clear that evidence used to prove inherency need not be public or prior art. *See Hospira,* 946 F.3d at 1329-30 (holding that "extrinsic evidence" used to prove inherency, such as patentee's own documents, need not be prior art); *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 1380 (Fed. Cir. 2003) (rejecting "the contention that inherent anticipation requires recognition in the prior art" and allowing use of post-critical date clinical trials to show inherency); *Telemac Cellular Corp. v. Topp Telecom, Inc.*, 247 F.3d 1316, 1328 (Fed. Cir. 2001) (relying on "[patentee]'s own documents" to prove inherency). As authorized by Federal Circuit precedent, Teva has properly used extrinsic evidence, including Plaintiffs' internal documents, to "help elucidate what the prior art [compound

[19] Plaintiffs cite Example 8b of the '251 patent, which purportedly gave a release rate of 3.4%, but that example is not an embodiment of the '251 patent claims because it does not contain starch. (JTX-1.8, Table 7.) In contrast, consistent with Hergesell's test results, every example containing both saccharose and starch as a stabilizer (i.e., Examples 8a, 8d, 8e, 8f, and 8g), as required by claims 29 and 30, has a reported release rate of 1.8% or lower.

[20] This Court denied in part Plaintiffs' motion *in limine* to preclude Teva's reliance internal documents and testimony to "fill in disclosures in the Hergesell 1 reference" (D.I. 277-15) and held that "Defendant may use the documents to show inherent properties, but it may not use the documents to supplement the disclosure beyond what is disclosed in the Hergesell 1 reference." (D.I. 282 at 5:12-15.) Plaintiffs renewed their objection at trial, this time arguing that Teva should be precluded from doing exactly that. While the Court admitted the inherency evidence, it invited post-trial briefing on the issue. (Tr. 315:14-23.)

tested in the ‘’442 patent and Hergesell] consisted of.” *See Hospira,* 946 F.3d at 1330. Teva respectfully submits that it should not be precluded from relying on this evidence to show that Hergesell’s data was based on Example 1 of the ’442 patent.

### D. Any Alleged Secondary Considerations Support Obviousness

At trial, Plaintiffs failed to prove that any alleged secondary considerations overcome the strong *prima facie* case of obviousness of the Asserted Claims. *See Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd*., 719 F.3d 1346, 1351-52 (Fed. Cir. 2013). If anything, the evidence relating to secondary considerations further supports a finding of obviousness.

#### 1. Plaintiffs Failed to Prove Unexpected Results or Long Felt Need

First, Plaintiffs failed to make a threshold showing of unexpected results “because the record is devoid of any evidence of what the skilled artisan would have expected.” *Pfizer v. Apotex,* 480 F.3d 1348, 1371 (Fed. Cir. 2007). By 2007, the market included several FDA-approved phosphate binders that were chewable, well-tolerated, and effective, with comparable loading; the prior art also described a high-load dosage form of iron oxyhydroxide that was reported to be safe, effective, and well-tolerated. (Tr. 731:15-732:2, 603:4-25; DTX-777.18; JTX-7.) Such known and expected properties do not support unexpected results. *See Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc*., 752 F.3d 967, 977 (Fed. Cir. 2014); *Abbott Labs. v. Andrx Pharm., Inc.*, 452 F.3d 1331, 1345 (Fed. Cir. 2006). They also show that the claimed invention did not meet any long-felt but unmet need. *See BTG Int'l Ltd. v. Amneal Pharm. LLC*, 923 F.3d 1063, 1076 (Fed. Cir. 2019) (no long-felt need when claimed invention was not “unexpectedly superior,” and prior art filled alleged need). Plaintiffs’ alleged safety concerns of metal toxicity and vascular calcification had already been addressed by lanthanum and sevelamer (both approved by FDA before 2007), which were shown in Dr. Rastogi’s studies to prevent calcification. (Tr. 538:20-

539:12, 542:2-5, 542:20-543:22.) Dr. Rastogi's admissions that lanthanum was effective and that he continues to prescribe sevelamer also show that there was no long-felt but unmet need for effective binders. (Tr. 508:22-509:18.) The evidence at trial confirmed the industry's view that Velphoro was "not expected to represent a quantum leap," as "[t]wo unsolved problems remain: the high pill burden (three to four per day) and gastrointestinal tolerance." (Tr. 547:13-548:13; DTX-1019.11.)

**2. Vifor Presented No Credible Evidence of Commercial Success**

Vifor also failed to show that Velphoro has been a commercial success. While Ms. Mulhern concluded that Velphoro was successful based on its performance from its March 2014 launch to September 2019, the data underlying these factors evidence poor performance and a ***lack*** of commercial success. For instance, Ms. Mulhern's data shows Velphoro captured only a 3.2% average prescription share ("middle of the pack"), only a 5.2% average share in her overly narrow calcium-free product submarket, and failed to meet internal projections by over 50%, with third-party analysts characterizing Velphoro's launch as "extremely limited" and disappointing. (Tr. 616:21-617:2, 630:15-631:17, 633:7-12, 744:21-745:17, 748:7-24; DTX-148-K; DTX-313-M; DTX-319.5; DTX-325.1; DTX-512.5; DTX-697.) Moreover, Velphoro's ***8.9% decrease*** in net sales in the first half of 2020—which Ms. Mulhern failed to consider—confirms a lack of success, especially when compared to the ***increase*** in Plaintiffs' other product sales over the same period. (Tr. 618:19-619:19; DTX-1063.2.)

**3. Plaintiffs Failed to Prove a Nexus Between Alleged Secondary Considerations and the Features of the Asserted Claims**

Plaintiffs' allegations of long-felt need, unexpected results, and commercial success have no nexus to the Asserted Claims. (Tr. 743:15-744:20, 748:2-6.) Plaintiffs' experts relied on three alleged benefits of the alleged invention: (1) "enhanced ease of administration" (e.g., size,

chewability, crushability, and palatability); (2) reduced pill burden; and (3) improved safety due to low iron release rate/toxicity. (Tr. 580:1-18, 583:23-584:4.) Because these features are not commensurate in scope with the Asserted Claims and did not drive demand for Velphoro, such evidence lacks a nexus and is not relevant here. First, there is no nexus to chewability, crushability, palatability, pleasant taste, "easily chewed," or a specific hardness or size, because none of the Asserted Claims recite any such limitation(s) and only claim 33 requires chewable tablets. (Tr. 523:9-525:20, 701:3-20, 739:16-740:3.) If anything, several were a substantial cause of patient discontinuation that impaired success. (Tr. 613:5-614:2, 747:9-14; DTX-532.4; DTX-330.13.)

Second, Velphoro's alleged reduced pill burden has no nexus to the Asserted Claims, which recite no limitations on size or the number of pills per dose. (Tr. 525:11-20, 701:15-17, 739:16-740:3.)[21] As Plaintiffs' formulation expert and 30(b)(6) witnesses explained, Velphoro's mixture of starches and powder flowability – likewise unclaimed – are responsible for any reduced pill burden. (Tr. 719:23-721:9, 739:16-740:3.) Finally, there is no nexus for limited iron release because Velphoro's prior art API is responsible for this feature. In fact, this feature retarded demand. Auryxia launched later but outperformed Velphoro due to the "apparent superiority" and beneficial iron release to address anemia. (Tr. 747:15-24, 623:3-626:16; DTX-300.19).

**4. The '442 Blocking Patent Diminishes Any Secondary Considerations**

The '442 blocking patent, which disincentivized others from developing the alleged

[21] Plaintiffs' Vifor's market research and shift in promotional campaigns confirm that "[e]fficacy drives behaviors, pill burden does not." (Tr. 603:12-25, 604:20-605:8, 614:23-616:7, 747:2-8; DTX-324.13; DTX-777.18.) And their witnesses affirmed efficacy as the primary and "lone attribute" sought by prescribers. (Tr. 507:20-508:5, 728:6-17.) Velphoro's iron oxy-hydroxide API was disclosed in the prior art '442 patent and is responsible for its clinical efficacy. (Tr. 743:25-744:5, 747:15-24, 289:3-16.) Thus, the necessary nexus has not been shown. *See Cubist Pharms., Inc. v. Hospira, Inc*., 75 F. Supp. 3d 641, 666-67 (D. Del. 2014) (no nexus for claims to dosing of product, not API, and API's properties were responsible for success).

invention, further limits any alleged considerations. (Tr. 744:6-15, 745:21-746:19); *Acorda*, 903 F.3d at 1339 (blocking patent "can discount the significance of" secondary considerations); *Galderma Labs., L.P. v. Tolmar, Inc.,* 737 F.3d 731, 741 (Fed. Cir. 2014) (same). The Orange Book provided notice to potential competitors that this earlier-issued patent covered Velphoro, and Plaintiffs characterized it as providing "market exclusivity." (Tr. 289:3-16, 636:6-637:8, 746:8-23; DTX-321.2-3.) The absence of other iron oxyhydroxide products in an already crowded market during its patent term, and the decisions by ANDA filers to forgo challenges to it, confirm that the '442 blocking patent diminished any limited relevance of the secondary considerations. (Tr. 745:21-746:23, 635:8-23; DTX-321.02.)

Thus, because no secondary considerations overcome the strong *prima facie* case of obviousness presented by Teva, the Asserted Claims are invalid as obvious over the prior art.

## III. CLAIMS 29 AND 30 LACK ENABLEMENT

To the extent the "essentially non-bioabsorbable" and "release rate" limitations are not obvious (or inherent) properties of the prior art, then the '251 patent does not enable claims 29 and 30 under 35 U.S.C. § 112. The enablement requirement is meant to ensure that the public is told how to carry out the invention, i.e., to make and use it. This requires the patent's disclosure to be "at least commensurate with the scope of the claims." *Amgen Inc. v. Sanofi,* 2021 U.S. App. LEXIS 3952, at *7 (Fed. Cir. Feb. 11, 2021). The fact that claims 29 and 30 broadly claim functional properties without any formulation-limiting details weighs heavily against enablement, particularly in view of Plaintiffs' arguments as to unpredictability, and the dearth of guidance in the '251 patent specification. *Id.* at *14-16 ("While functional claim limitations are not necessarily precluded in claims that meet the enablement requirement … the use of broad functional claim limitations raises the bar for enablement.") (citing *In re Wands*, 858 F.2d 731, 736–37 (Fed. Cir.

1988) (Factors 1, 2, 3, 5)). In this case, a POSA is faced with an undue level of experimentation that requires experience and training outside the level of skill, and without sufficient guidance in the prior art. *Wands,* 858 F.2d at 737 (Factors 4, 7, 8).

With respect to claim 29's "essentially non-bioabsorbable" limitation, experts on both sides agreed that the '251 patent did not provide "any guidance" or working examples as to what constitutes a "clinically significant" amount. (Tr. 121:19-23, 327:11-16, 376:19-378:24.) This weighs strongly in favor of a finding of non-enablement. *See Wands,* 858 F.2d at 737 (Factors 5, 6); *Impax Labs., Inc. v. Aventis Pharm., Inc.*, 545 F.3d 1312, 1314-15 (Fed. Cir. 2008). Furthermore, as to unpredictability, the testimony of both sides' experts was that numerous factors (inflammation, blood loss, diet, medications, form of iron, infections, etc.) could affect what would be considered a "clinically significant" amount of absorption, as well as that such factors generally vary from patient to patient and would be unpredictable to a POSA absent *in vivo* testing of each patient. (Tr. 122:22-124:2, 125:11-16, 134:25-136:3, 218:16-221:5; DTX-67.200 ("more pronounced increases in ferritin … appeared to be influenced by the occurrence of infections in some subjects.").) Such unpredictability is a keystone of non-enablement, especially considering the complete absence of guidance in the '251 patent. *See Wands,* 858 F.2d at 737 (Factors 2, 3); *Enzo Life Sciences, Inc. v. Roche Molecular Sys.*, 928 F.3d 1340, 1347-48 (Fed. Cir. 2019). In view of this unpredictability, and the undisputed need to undertake the substantial burdens of *in vivo* testing of each and every individual patient, a POSA would have to engage in extensive and unduly burdensome testing in order determine whether a particular product, when administered to a particular patient, would satisfy the claimed function. *Id.* (Factors 5, 6); *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1385-86 (Fed. Cir. 2013) (not enabled due to large number of candidates within claim scope, and lack of guidance, necessitating undue experimentation to

screen each candidate to determine which ones exhibit claimed functionality). The non-enablement is further compounded because such testing and determination is not within the skill of a POSA. *Amgen,* 2021 U.S. App. LEXIS 3952, at *17-18; *Wands,* 858 F.2d at 737 (Factor 7).

Similarly, Plaintiffs' argument that the ***brand*** of starch may impact the release rate confirms that claim 30 is not enabled. The '251 patent provides no guidance concerning how the countless number of suppliers and types of starch would impact the claimed iron release rate for any particular sucroferric oxy-hydroxide product absent testing of each one of them. (Tr. 377:19-378:24.) Plaintiffs' attempt to prove on cross-examination (Tr. 380:9-386:7) that there is a ***single*** embodiment in the patent that generally identifies ***one*** brand of starch (Tr. 379:16-21) does not suffice for enablement. *Amgen,* 2021 U.S. App. LEXIS 3952, at *13 ("[I]t is important to consider the quantity of experimentation that would be required to make and use, not only the limited number of embodiments that the patent discloses, but also the full scope of the claim."). Thus, to the extent Plaintiffs' starch brand argument is credited, the level of experimentation that would be required of a POSA in order to practice the full scope of these claims would be undue. *Id.* at *18 (holding that "'substantial time and effort' would be required to reach the full scope of claimed embodiments" where "[t]he functional limitations…are broad, [and] the disclosed examples and guidance are narrow"); *Enzo*, 928 F.3d at 1345-48 (patent failed to teach whether the many embodiments would exhibit the claimed functionality). (Tr. 327:17-328:2, 377:19-386:7.)

Claims 29 and 30 should found invalid as obvious and for lack of enablement.

## IV. CONCLUSION

Teva respectfully submits that the Court should find the Asserted Claims invalid under Section 103, and/or under Section 112, based on the clear and convincing evidence of obviousness and lack of enablement of the claimed subject matter.

*/s/ Nathan R. Hoeschen*
John W. Shaw (No. 3362)
Karen E. Keller (No. 4489)
Nathan R. Hoeschen (No. 6232)
SHAW KELLER LLP
I.M. Pei Building
1105 North Market Street, 12th Floor
Wilmington, DE 19801
(302) 298-0700
jshaw@shawkeller.com
kkeller@shawkeller.com
nhoeschen@shawkeller.com
*Attorneys for Defendant Teva Pharmaceuticals USA, Inc.*

OF COUNSEL:
Scott J. Bornstein
Richard C. Pettus
Jonathan D. Ball
GREENBERG TRAURIG LLP
MetLife Building
200 Park Avenue
New York, NY 10166
(212) 801-2172

Jonathan R. Wise
GREENBERG TRAURIG LLP
2700 Two Commerce Square
2001 Market Street
Philadelphia, PA 19103
(215) 988-7850

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